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A C&EN SPECIAL ISSUE

AIDS The science of a human tragedy

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News of the Week

■ **EPA extension of deadlines for meeting clean air standards draws strong criticisms.** **Page 4**

■ **Hoechst Celanese plant in Pampa, Tex., is site of two explosions and ensuing fire that killed three people and caused extensive property damage.** **Page 4**

■ **Genentech receives FDA approval to market blood clot-dissolving drug, Activase.** **Page 5**

■ **In Bhopal case, Union Carbide and the Indian government fail to reach a settlement by court-issued deadline.** **Page 5**

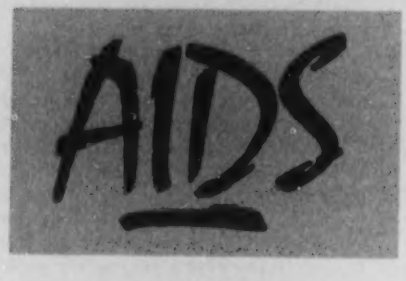
■ **Clayton Callis, vice president of environmental consulting firm Chelan Associates, has been elected ACS's 1988 president-elect.** **Page 6**

Cover: Portion of an enormous quilt that commemorates more than 1900 persons who have died of AIDS. The quilt was unfurled in a ceremony on the Mall in Washington, D.C., in October. Photo by C&EN's Ron Dagani

Letters 2

Concentrates
Business 9
Government 10
Science/Technology 11

The Departments
Books 69
Awards 71
Newscripts 88



The tragic story of AIDS is a maelstrom of scientific, public health, social, moral, and policy issues. **Page 12**

The Molecular Biology

Scientists worldwide mount an intensive research effort in their quest to understand the structure and genetics of HIV, the virus that causes AIDS, and identify weaknesses that might lead to therapies. **Page 14**

The Search for Vaccines

Variety of AIDS vaccine strategies are being investigated and a number of potential vaccines have been developed but success, as yet, seems on the far horizon. **Page 27**

The Problem of Diagnostic Tests

Researchers' goals for second-generation HIV diagnostic tests include greater sensitivity and specificity, while improving on speed, simplicity, cost, and safety. **Page 35**

The Quest for Therapy

Dozens of potential drugs are being tested as either antiviral or immune-restoring agents, but so far the only approved therapy is the high-priced drug zidovudine. **Page 41**

The Public Health Challenge

Public health issues associated with AIDS engage the country in legal and ethical exchanges involving testing and education, pitting the public good against individual rights. **Page 50**

The Government's R&D Policy

Federal government's initial stance on AIDS begins to change as research and development funds become available, and policy "system" is formulated. **Page 59**

The Business Response

The business community is actively involved in the development of vaccines, drugs, and diagnostic tests, despite scientific, medical, and business uncertainties. **Page 66**

Chemical & Engineering News

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LETTERS

Improving public image

SIR: I have just read the official statements by the ACS presidential candidates and have dutifully voted. Both candidates sound like fine persons and our society is lucky that such people have a desire to serve.

I am writing this letter for the many thousands who wish to beg and plead that the winning candidate not increase the dues, which seem to creep incessantly upward. Some of us are definitely not as well off as others and the yearly dues bill does hurt.

I agree that much needs to be done and our public image needs much help. It will all take money. Please be creative when it comes to raising funds. Put the strong arm on industry, which is fundamentally responsible for the image problem we have. Convince industry that they help themselves by helping us. Industry should donate big money to ACS. The time for this idea has come.

My final thought has to do with how to spend the money to improve our public image. Spend the money on truthful things and not on slick advertising that the public has become too sophisticated to swallow. As scientists we must all latch hold of the new truth—the biosphere of our Earth is finite and we must stop harming it. We must push for new laws and agreements that allow competitive capitalism to continue without a dead environment as the side effect.

Dennis Baker
Makawao, Hawaii

Nonscientific programs

SIR: At the recent ACS Council meeting in New Orleans, I raised the question of the suitability of permitting four firms to peddle schlock to registrants and attendees at the exposition. I now note that the chairman of the Membership Affairs Committee lists three criteria for determining whether nonscientific programs shall be considered for offering to members (C&EN, Aug. 31, page 47). These are, briefly, availability to the majority of members from other sources; expense to the society; and income to the society—and they require a "No," "No," and "Yes" answer to be approved.

On this basis, I realize that relatively few ACS members have access to a world-class symphony; can we then sponsor a speakers bureau tour for Solti and the Chicago Symphony? Perhaps we can look forward to Bruce Springsteen appearing before the East Podunk Section. I may find it not only inconvenient but a bit embarrassing to have to travel quite a distance to purchase an X-rated video. Could C&EN add a lonely hearts section to its very productive want-ad department?

In discussing the matter with other councilors after the meeting, I find that there are some who feel strongly that the "Travel Department" does not belong in our programs. Some others, possibly fewer in number, feel that peddling a charge card does not come under the mandate of our charter. Still others may object to one or all phases of the insurance program. Although there obviously will not be any unanimous opinion on where we should draw a line, I believe that at least the majority of our members feel that there should be a line.

James J. Doheny
Brookfield, Ill.

Doctorate in chemical research

SIR: A novel concept, which proposes the awarding of an alternate doctorate to qualified chemical researchers by ACS, is presented in the letter of David R. Schryer (C&EN, March 16, page 33). This idea is both timely and meritorious. It is fraught with promising possibilities and deserves serious consideration. Responding to Schryer's letter, Kurt J. Rorig (C&EN, May 25, page 2) suggests the granting of a certificate entitled, "Diplomate in Chemical Research (Dipl. C.R.)." This terminology is intended to avoid interference with the domain and authority of a university to grant the degree of Ph.D. and also the honorary Ph.D. Rorig's certificate of Dipl. C.R. seems reasonable, but it appears to dilute to some degree the honor and prestige of the Ph.D.

Consequently, the problem of finding a more suitable designation for chemical research achievement (particularly in the industrial field) would boil down to a consideration of the difference between granting a degree and a title. There is a specific difference. Then too, since the Ph.D. is considered to be a research degree, then the alternative would be a research title. Accordingly, I wish to suggest the use of the wording, "confer the title of Doctorate in Chemical Research (D.C.R.)" in an appropriate certificate granted by ACS. I am inclined to believe that it would be in the domain and privilege of ACS to establish and grant a certificate of this kind to its qualified colleagues. This privilege would be a plus to the prestige of ACS, and also

The Government's R & D Policy

After a slow and contentious start, the federal R&D effort aimed at combating AIDS is taking shape, as funds flow and organization evolves

Wil Lepkowski, C&EN Washington

Of all the science policy issues the federal government and the scientific community have had to deal with over the years, none has touched raw nerves so much as the scourge of AIDS and the drive to halt it. Acquired immune deficiency syndrome is a domestic and international disaster.

Hope persists that human immunodeficiency virus (HIV) will continue to keep its distance from the general heterosexual community, only marginally affected up to now. But the heterosexual middle class in the U.S. could be quickly galvanized if the virus does begin to sweep through that population. It is a prospect scientists, policymakers, and politicians dread.

The struggle against AIDS, therefore, is a huge challenge for science, and an enormous policy task.

After early Administration confusion, infighting, and failure to recognize the urgency of the epidemic, the funding is now beginning to pour in. When Congress gets through with appropriations at least $1 billion will be approved for the current fiscal year in funds for research, treatment, diagnosis, and education by the U.S. government. The sums will likely rise year by year and approach a total of $2 billion if scientists involved in advisory roles get their way.

The basic fact about AIDS transmission, however, is the one Mr. & Mrs. America find most difficult to digest: that it was spread throughout the country mainly by anal intercourse between promiscuous homosexuals. Thus the major barrier to a national AIDS "dialogue" is the public's traditional antipathy toward that group and skittishness concerning explicit sexual descriptions in educational materials. Moralistic attitudes were so strong that only this year did President Reagan deliver an address on the specific topic of AIDS.

Conservative politicians and the Administration want AIDS policy to reflect traditional Christian moral values and not be seen as condoning homosexual practice, premarital sex, or drug abuse. Unfortunately, those "values" sometimes take the politically inflammatory form of outlawing private behavior and quarantining AIDS patients.

Homosexuals, meanwhile, want attention directed more at the need to curb and eliminate the virus. Scientists want to get on with the basic research, the search for a drug, and with straight talk on changing sexual behavior and the practices of drug addicts to closet the virus and slow down its spread.

Because of President Reagan's difficulty in insisting that his Administration speak with a single voice on the subject, most observers feel that AIDS will become even more political than it already is, drawing scientists more deeply into the fray. "It's bound to be a major issue in the election; I can't imagine it will not be," says Institute of Medicine president Samuel Thier. The institute has been at the forefront of AIDS policy issues, with a landmark report issued last year in combination with the National Academy of Sciences and several meetings on the subject. He expects political controversy to intensify.

One Republican candidate, Pat Robertson, for example, told a Rockford, Ill., audience late last month that scientists were "misleading the public" in saying AIDS is spread only by sexual contact. "I don't think scientists are telling the truth about AIDS," he said. In arguing in favor of such measures as possibly quarantining AIDS victims and making AIDS testing mandatory for high-risk groups, Robertson said, "I do not know of any virus that has a civil right." Robertson was not in fact reporting correctly the judgment of scientists. Thier's Institute of Medicine Committee for a National Strategy on AIDS has said AIDS is spread not exclusively,

Fauci: perceptual gaps should close

only mainly, by sexual contact. In its report it listed all the other means of transmission.

That is why the biomedical community feels that it must be seen as a sea of calm purpose as the AIDS policy debate matures. "The perception is just as important as the reality," comments David Baltimore, director of the Whitehead Institute for Biomedical Research in Cambridge, Mass. Baltimore meant that the public must have confidence that the scientific community is working in the interest of the public in a unified attempt to develop drugs and vaccines, and to inform the public in plain language on the facts of the disease and on new developments as they occur.

That community got off to a credible start with the release last September of the Institute of Medicine/NAS report, "Confronting AIDS," seen as the definitive policy document on the subject. It was hoped that the study would alleviate the poor press that scientists received in the early 1980s, when the AIDS outbreak was taking the form of a national emergency.

Then, AIDS news was monopolized by conflicts between French scientist Luc Montagnier and his American counterpart, Robert C. Gallo of the National Cancer Institute, over discovery of the HIV virus, as well as fierce infighting between NCI and the Centers for Disease Control over research leadership. Since then, the National Institute of Allergy & Infectious Diseases (NIAID), headed by Anthony S. Fauci, has become the lead research agency in the AIDS program and intragovernmental tension has decreased significantly.

With the major bureaucratic battles pretty much over, an AIDS policy "system" is slowly taking shape. It has four major components: research, the drug and vaccine development related to it, education, and testing. All are related. Political ideology has an impact on all of them, especially infusing education and testing. But whereas education and testing issues remain unresolved and await legislation and policy, the technical aspects are pretty clear-cut: find treatments and a cure for AIDS. The major issues include:

NIH funds network of AIDS centers across U.S.

AIDS treatment evaluation units
National cooperative drug discovery groups
AIDS clinical studies groups
NIAID vaccine evaluation units

AIDS treatment evaluation units

Memorial Hospital for Cancer & Allied Diseases, New York City
Johns Hopkins Hospital, Baltimore
U of Washington, Seattle
U of Miami, Miami
Massachusetts General Hospital, Boston
Tulane U Medical Center, New Orleans
Institute for Immunological Disorders, Houston
San Francisco General Hospital, San Francisco
Albert Einstein College of Medicine, New York City
New York U Medical Center, New York City
U of Minnesota Health Science Center, Minneapolis
Duke U Medical Center, Durham, N.C.
U of Rochester, Rochester
UCLA School of Medicine, Los Angeles
U of Pittsburgh, Pittsburgh
USC Medical Center, Los Angeles
Stanford U School of Medicine, Stanford
Mount Sinai Medical School, New York City
U of California, San Diego

National cooperative drug discovery groups

Memorial Sloan-Kettering Cancer Center, New York City
Duke U Medical Center, Durham, N.C.
Purdue U, West Lafayette, Ind.
U.S. Army Medical Research & Development Command, Fort Detrick, Md.
U of Texas Medical Branch, Galveston, Tex.
Stanford U School of Medicine, Stanford
Biogen, Cambridge, Mass.
Dana Farber Cancer Institute, Boston
U of Miami School of Medicine, Miami
George Washington U School of Medicine, Washington, D.C.
Emory U School of Medicine, Atlanta
State U of New York School of Medicine, Buffalo
State U of New York School of Medicine, Stony Brook
U of Alabama School of Medicine, Birmingham
City of Hope National Medical Center, Duarte, Calif.
Worcester Foundation for Experimental Biology, Worcester, Mass.

AIDS clinical studies groups

U of Texas Health Science Center, San Antonio
U of Massachusetts Medical School, Worcester
New Jersey Medical School, U of Medicine & Dentistry of New Jersey, Newark
Milton S. Hershey Medical Center, Hershey, Pa.
Ohio State U Medical Center, Columbus, Ohio
U of Cincinnati College of Medicine, Cincinnati
Robert Wood Johnson Medical School, U of Medicine & Dentistry of New Jersey, Piscataway
St. Luke's/Roosevelt Institute for Health Sciences, New York City
Indiana U School of Medicine, Indianapolis
Case Western Reserve School of Medicine, Cleveland
U of North Carolina School of Medicine, Chapel Hill
Children's Hospital, Boston
Cornell U Medical College, New York City
Northwestern U Medical School, Chicago
Washington U School of Medicine, St. Louis, Mo.
George Washington U, Washington, D.C.
State U of New York, School of Medicine, Stony Brook

NIAID vaccine evaluation units

U of Rochester, Rochester
U of Maryland, Baltimore
Johns Hopkins U, Baltimore
Marshall U, Huntington, W.Va.
Vanderbilt U, Nashville
Baylor College of Medicine, Houston

• Funding. How much is enough? The Institute of Medicine/NAS report says a billion dollars each for education and research should be sufficient. The Administration says that's too much right now. Congress leans toward those levels.

• The federal research effort. NIAID is the lead agency for the war on AIDS. It has quickly shot up from a small agency with a $300 million budget to one overseeing $600 million in research and drug and vaccine development for all infectious diseases in addition to AIDS. Is it up to the effort? New laboratories and clinical centers must be built. Scientists think the Administration is moving too slowly to bring them into operation.

• Overall AIDS research management. Should it be led by an AIDS "czar?" How tightly should it be "managed?" What are the areas of management needed? Would such management interfere with scientific creativity? Should an outside commission oversee any such effort?

• Drug development. Is government-industry-university effort coordinated well enough? At the moment the system of moving new chemical entities from the idea stage on up through characterization, evaluation, testing, and approval is still under development. Small research firms complain that their ideas are given insufficient hearing. Large companies think NIH is playing too heavy a role in drug development and are tired of hearing academic scientists question the industrial profit motive. Questions over secrecy and patent rights persist. Few understand the role the Food & Drug Administration should play in the development work.

Almost $1 billion ($962 million) has been spent on AIDS research and education since the disease was first funded specifically in 1983. But last month, the Senate approved a $946 million AIDS package, including $310 million for education efforts at CDC. Included separately are bills for testing.

Congress, however, is still learning how to respond legislatively to AIDS. It was only this year that AIDS became part of the authorization process, the mechanism by which Congress sets funding priorities area by area. Previously AIDS money came solely through the appropriations process, leaving distribution and priority setting pretty much to the agencies themselves. With authorization, Congress obtains open access to debate over important areas of emphasis.

The agency most involved in the basic decisions over funding is, of course, the Office of Management & Budget. There, a series of analyses of funding needs by the various agencies is continuing as the Administration's fiscal 1989 budget is being prepared for the President. "All this is going on while the fiscal 1988 budget is still unresolved, so we don't know what base to work from," says one OMB source. "Besides that," he says, "there are all kinds of authorizing bills that have not been acted on, including AIDS research, testing and confidentiality, drugs and AIDS, and abandoned infants."

The Administration is aiming for no more than a $791 million total AIDS figure for fiscal 1988. But Congress already is pushing for $1 billion. Requests from the relevant agencies for fiscal 1989 already total "well over" $1 billion, sources say.

"We're asking where the resources are going to come from to absorb the increases in AIDS money," says the OMB source. "We're looking at the morbidity and mortality of AIDS, and seeing that it's a lot less than other diseases. I don't think people are analytical enough yet; they're too emotional. We're in a situation now where we're dumping money into AIDS, where we're playing 'Can You Top This?' A cynical way of looking at it is that you can frighten people into starting a lot of base activities just by using the word AIDS."

OMB also says it is concerned with waste. "There's a lot of slop in the system that no one wants to deal with," he says. "No one really asks whether the programs are effective and whether they have goals. You never get those kinds of questions asked at Congressional appropriations hearings. I don't think the question of quality work will be dealt with analytically as long as AIDS continues without a cure."

Although the Administration at first was highly reluctant in face of pleas from scientists at CDC to open its purses in pursuit of AIDS treatment and cure, it is showing much less reluctance now. "We'll spend every dollar we can come up with on research for a cure, for vaccines, and for drugs to treat AIDS," says Gary L. Bauer, assistant to the President for domestic policy.

Bauer more recently has become deeply involved in the total battle against AIDS. Currently he is seeking a more precise understanding of the technical issues and the management strategies. Scientists are happy about that, though they continue to be put off by what they feel is Bauer's overly conservative rhetoric.

However, whether Bauer will agree with bills like the one sponsored by Edward M. Kennedy (D.-Mass.) is questionable. Kennedy calls for a network of officially designated AIDS research centers around the country, just as there are centers on cancer and heart disease. His legislation, moreover, would raise NIAID to an administrative level equal to that of NCI, which runs the war on cancer with a budget independent of centralized National Institutes of Health control.

NIAID's research strategy has six major components aimed at understanding:

- The natural history and epidemiology of the disease.
- The nature of the virus itself.
- The pathogenesis of AIDS.
- Drug therapy.
- Vaccine development.
- Rebuilding of the immune system.

The managerial aim is to integrate all those activities among industry, government, and academia and their diverse values and approaches. The effort is naturally very costly, so costly that enormous pressure exists to manage it well. Not only are new ideas needed in basic studies, but resources in the form of people and facilities are in immediate demand.

Nor is that research routine, especially the closer new ideas get to clinical applications. "Clinical trials don't fit easily into the context of routine clinical practice," says Jerry

Friedland of Montefiore Medical Center in New York City. "We need new facilities within institutions that are already taxed in terms of space and personnel. We need to recruit and train new personnel in an environment in which there are increasing recruitment difficulties for staff to work with AIDS patients." Within all that, he adds, is the need for systems for the collection of specimens, for information flow, for communication between investigators, for various medical services.

Adds Irving L. Weissman of Stanford University, "Although the research carried out to date has been of the highest quality, nowhere near the enormous talent pool available to work on this disease has, in fact, been effectively recruited."

At Stanford University, "and probably elsewhere," reports Weissman, there is no HIV containment facility available to qualified investigators who wish to follow their own lines of inquiry; no fully developed high containment animal facility to house mice or other [laboratory] animals; and no funds to build such facilities for common use by qualified investigators. Many outstanding groups continue to work in overcrowded and underequipped facilities."

Friedman and Weissman made their remarks at a lively two-day meeting on AIDS drug development and policies last August at the Institute of Medicine.

Even the idea of throwing money at AIDS—a concept OMB abhors—makes some sense. Says biochemist Paul Naylor of George Washington University: "We need a tripling of the research budget on AIDS to really ensure that truly new ideas will be funded. A doubling would allow funding of only further traditional ideas, since not enough of them are funded in normal budget years. A tripling is when the system really begins generating novel, nontraditional ideas. And that is what's beginning to happen now."

To Weissman, the talent pool is available. But to Naylor there are shortages, for which he blames the government. "The number of scientists to study AIDS is limited by the number of people we trained 10 years ago," he says. "Over the years we have cut the number of scientists we've been training. One of the places to get scientists is from industry. But the biotechnology industry bought up tremendous numbers of academics who would have been in universities. Now, if you want to tap their abilities, you have to pay a fee to their companies so they can get a payback."

Misperceptions abound, depending on whether one is already a recipient of AIDS research funding, or hoping to get in. James D. Watson, director of Cold Spring Harbor Laboratory, charged NIH last August with closing off the field to those researchers on the outside. "You either become part of a formal agreement or you are not part of the effort," said Watson.

But Harvard University's William A. Haseltine, one of the early AIDS researchers, disagreed. Said Haseltine, "People have been invited in many, many times and have chosen not to enter. Scientific leadership has been lacking from our own traditional leaders in molecular biology, biochemistry, and virology."

Some scientists are complaining that the AIDS research effort, although necessary, has been undertaken at the expense of basic biomedical studies. Not only that, but research funds have shifted from so-called investigator-initiated research to studies that NIH suggests. NIH scientists sometimes find themselves the target of academic arrogance. "Most highly intelligent and accomplished investigators," commented one medical school researcher at the Institute of Medicine meeting, "do not wish to surrogate their own ideas and projects to those dictated and administered by other scientists—most of whom may not be as bright or as accomplished as the external investigator."

These are only a sampling of the complications involved in the AIDS crisis. OMB sources say the Administration is still far from organized for any such massive campaign against AIDS. "The AIDS war is more like Vietnam, where you can get mired in little battles," says one official. "Polio and measles required a vaccine; you could deal with that. But like in Vietnam, when you get to AIDS, you don't have to be very bright to just know the situation isn't going to be dealt with very easily."

The Institute of Medicine's Thier agrees. Infectious diseases hadn't been considered anything near a crisis field with tragic and fascinating mysteries. The major infectious diseases had long been under control—until AIDS. Now battles need to be fought in guerillalike fashion against an often invisible enemy. No wonder Thier believes new coordinating ideas are needed.

"We have a tremendous health system in this country— the universities, the Public Health Service, and the pharmaceutical companies," he says. Health care funding is by and large adequate through medicare and other health insurance. The performances are superb. FDA approved the AIDS test in three months. AZT was approved in short order. Those groups were mobilized and are doing a terrific job.

"But still, there is no coordination among the Department of Health & Human Services, the Defense Department, and the departments of Education, of Justice, and of State. There needs to be someone processing information and looking at the gaps. The last thing I want is an administrative layer over NIH and CDC. Instead, I'd rather see a group saying things like 'Did you think of this line of research?' It would have the credibility to point out areas not being given enough attention."

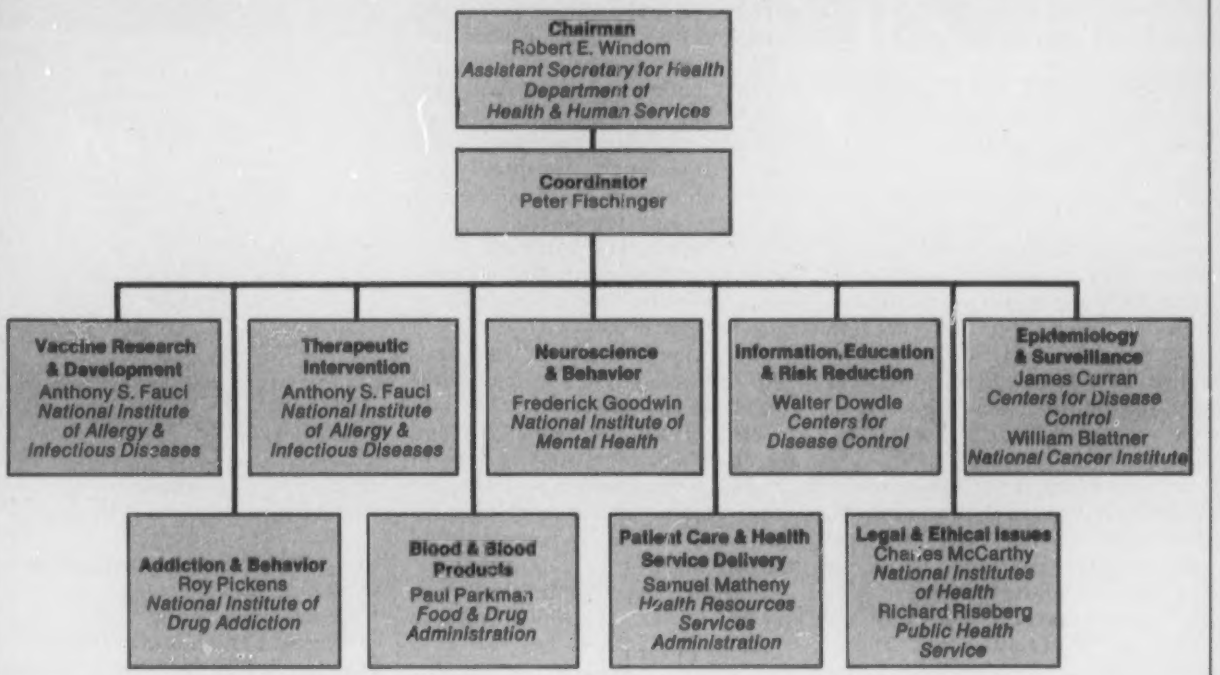
That essentially is what the Institute of Medicine and NAS recommended and what the President's commission on HIV could well recommend when it makes its report

Federal AIDS funding has risen sharply since 1984

$ Millions	1984	1985	1986	1987	1988*
Public Health Service	$61	$109	$234	$494	$791
Federal medicaid share	0	0	130	210	375
Veterans Administration	6	12	24	30	44
Department of Defense	0	0	79	74	52

Note: Fiscal years. a Estimated. Source: Office of Management & Budget

Public Health Service Task Force on AIDS attempts to coordinate AIDS effort



to President Reagan next June. Congress certainly is pushing for it in various bills. It is what the scientific community within the government was hoping Reagan would do immediately after the Institute of Medicine/NAS report came out. But to their disappointment, the President did nothing. The Office of Science & Technology Policy, in fact, made an attempt to inform the White House after a briefing by NIAID. But a list of recommendations brought to the East Wing by science adviser William R. Graham at the end of last year met only with silence.

Since then, Graham has been assigned no influential role in AIDS policy. An interagency group—the Federal Coordinating Committee on AIDS Information, Education, & Risk Reduction—which OSTP would normally head, is chaired instead by Department of Health & Human Services assistant secretary Robert Windom. Although Windom has spoken out as strongly as Surgeon General C. Everett Koop on the education/information issue, insiders say the committee he heads operates at too obscure a level to convince the President of the need for a White House consensus.

On the education issue, Thier thinks the scientific establishment has received a rude awakening on AIDS in that its best considered opinions were not heeded. "It's rare enough to have independently a consensus by the Institute of Medicine, the Public Health Service, and the American Medical Association on a set of policies. But to see them rejected as being too political is the awakening. The education effort has been bogged down because it is a sex and drug issue."

The testing recommendations met the same fate. Voluntary testing for large numbers of people was recommended by the panel, but top Administration sources and conservative members of Congress prefer a more mandatory approach. To Thier, the voluntary approach still makes very good sense. "Of the sites for voluntary testing that were set up, all have been oversubscribed. There were waiting lists of two to three months. And despite the fact that we cannot meet the demands for voluntary testing, people are still only talking about mandatory testing. The whole thing is bizarre."

Thier says an outside committee above the ideological battleground is absolutely needed to oversee the broad effort. "This is not an ideological process," he says. "It's a disease that's eating up a lot of people. It needs a mechanism to pull people together so that the public knows someone is in charge and is paying attention. The public doesn't know who to believe, who to trust."

Rochelle Diamond, an AIDS researcher at California Institute of Technology and spokesperson for the National Organization of Gay & Lesbian Scientists & Technical Professionals (NOGLSTP), says the group should be paying particular attention to coordinating the growing number of AIDS drug development laboratories. Too many are laboring in the dark, she believes. "Any coordinator," she says, "should be receiving information and disseminating it so that all the labs know who is doing what. We should be having more national meetings and having frank discussions about what is going on. Even today some people are complaining that the Na-

tional Cancer Institute is not sending them the virus. And that brings up the issue of whether the distribution and cultivation of the virus should be controlled."

NIAID's Fauci says that such accusations are commonplace but wrong. And he is quick to defend the cancer institute's Robert Gallo, who has received most of the criticism. "Bob has heard about these accusations and he has compiled a list of people he has sent reagents to. It's easily an inch and a half thick. What I think is going on is, first, that you have personal antagonisms and rivalries between people in the field and, second, that he can be a difficult person to deal with. But reagents are not being withheld."

But more important than issues of personalities are the communication gaps between NIH and academic researchers. Fauci points out that misperceptions between NIH and researchers not yet fully involved in AIDS studies stem simply from unfamiliarity with the existing network and its structure. "The meetings and committees they say we don't have," he says, "have in actuality existed for months." As more scientists move into AIDS research, the perceptual gaps should close, he says.

Diamond herself admits things are getting better. "Although we need coordination, people are becoming aware. Congress knows we need the money. And we need to know that it gets to the right places and that the effort continues on a rational basis. But the work is slow and painful and we're losing a lot of lives. People are losing their friends."

One phenomenon that coordination could improve is the personal and professional interaction of scientists in the field. Right now there are difficulties here and there unrelated to the controversies that always seem to swirl around Gallo. Ian Brick of HEM Research Inc., which with Du Pont is developing the AIDS drug ampligen, speaks from the industry side. "A problem a lot of the companies are having," he says, "is the feeling of distrust toward the commercial people by those at NIH. They believe the companies have a lot of money and are in it to make money if they develop something. There's no trust between them. Most things come from commercial opportunities, and the bridge to that perception is not totally in place."

What isn't helping in this new interaction is the secrecy surrounding the best developments, stemming not so much from purely scientific competition but from the race to patent and commercialize new developments. Any successful treatment for AIDS, much less its cure, is an invention worth hundreds of millions of dollars.

"No question about it," says GWU's Naylor. "The sharing of data and ideas is significantly less than in other fields I've been in. I had never before seen such a lack of candor in discussing new ideas and the sharing of approaches. What we have is a series of close-mouthed relationships.

"Part of the problem is that people at NIH can take consulting fees from industry. Now they can have a relationship with a corporation, and that may not be so good an idea. Scientists at NIH aren't sharing ideas so much anymore, not even among themselves. For example, even to this day we haven't seen any data on the vaccine being developed by MicroGeneSys and NIAID. The scientists are not talking about it and their collaborators also are reluctant."

Now, Naylor says, relations among academia, NIH, and industry are an absolute necessity. "But as soon as you do that, you open the Pandora's box of secrecy and suspicion," he says. "Reagents are available only at a price. Antibodies to pieces of the virus are available only at a price, even though these agents were developed with the help of NIH scientists."

Fauci admits there is a problem. Competing university-industry-government consortia are now a reality. It's now standard operating procedure that scientists from a drug company, a university, and an NIH laboratory form a single developmental team. And such teams are competing. Fauci says information does tend to get withheld pending the filing of a patent. "Maybe ways can be found to accelerate the filing procedure," he says. "It's something the patent attorneys need to work out."

Thier: new coordinating ideas needed

In the end, though, a sense of compassion and ethics, whatever its likelihood, will have to be trusted to rule. "Drugs and devices to cure disease and relieve suffering should not be viewed as commodities," Montefiore's Friedland says, "but as a special sort of social good. Political economists, health policy makers, and industry are under a challenge to ensure that market forces do not deprive AIDS patients of potentially lifesaving resources."

Of all the aspects of the AIDS effort, drug development is the most frantic and confusing because it's so interconnected with the research effort. NIAID is essentially running the drug development effort, in a huge buildup of manpower and facilities, and thus operating in a mood of urgency and a continuing atmosphere of controversy.

NIAID is new at the game of drug development, however. NCI, on the other hand, has been clinically screening promising cancer chemotherapy agents for two decades through NIH's clinical center and a network of clinics around the country. So some of that NCI expertise is being lent to NIAID for the duration. For example, NCI is doing almost all of the in-vitro screening of new chemicals. And some of NCI's top drug experts have come over to NIAID to direct drug development.

Under NIAID, AIDS treatment evaluation units are being set up as funding continues to soar. Nineteen exist so far, with more to be established. A network of AIDS basic research centers will be established, similar to the national cancer centers spread around nationwide. Cooperative drug discovery groups and clinical studies groups also have been established. The institute is inviting researchers to submit applications for research and has to process applications and rule on new ideas as well as conduct its own research at the same time. NIAID is in the unique position of having to oversee basic research directed almost solely at therapy.

Naturally, many have criticisms of NIAID's efforts. "Right now it seems like they are just taking their own favorite drugs and forcing their network to look only at them and not do their own development work," says Naylor. "NCI has always allowed their collaborative networks to make their own decisions. But NIAID is much more centralized."

Paul Volberding of the University of California, San Francisco, another of the scientific AIDS pioneers, has related criticisms. He believes the movement of some important drugs into the research and evaluation system is being inhibited by current procedures. "There is a good deal of suspicion that scientific fads or commercial biases have a role in how drugs are developed," he pointed out at the Institute of Medicine meeting. "There is the feeling that clinical trials take too long and there is the common feeling that placebo trials are unethical, given the natural history of the virus."

Commercial biases derived from intense competition are indeed a reality and one that is difficult to get around given the current market system. "You can talk about drug development in a lot of ways," responded NIH's Wolfgang Joklik. "But as soon as someone out there identifies a new lead compound in any one area, the major fear that most companies have is that any other organization is going to 'derivatize' that compound and maybe beat them to the market with it. So patent rights aren't the only concern. It is secrecy in general that is raised."

Despite closer than ever collaboration between industry and academia in AIDS, the traditional conflicts persist. Joklik believes part of the problem lies in the "naiveté of academic institutions regarding drug development." He says the problem rises from several directions. "There are a lot of people who really think that the companies should pay through the nose up front. It is an unrealistic expectation. Related to that is the attitude of peer review. Many of the aspects of drug discovery and development are seen by the academic community as not being the most innovative, as being somewhat redundant at times. So getting through peer review presents a problem. To rectify that we have tried to get more people from industry on our review panels and to provide better education on what this program is about."

FDA comes under its share of pressure as well. Says Naylor: "To the investigator the major problem is that there is no clear policy guidance. You never know which side of the question FDA is going to come down on. Traditionally it was easy to go to Phase 1 of testing. What we feel is happening now is that FDA is adding an additional factor in trying to predict probability of the success of a procedure. That means that in a sense they are trying to weigh the efficacy without giving us the chance to show that it might be safe and effective. Also, we feel that FDA is not responding as quickly as we'd like to the expedited review process."

Some smaller companies think NIAID is showing favor to the large pharmaceutical firms. Comments a Capitol Hill staffer, "Small companies are saying that no matter what they do, they can't get NIAID's attention. The upshot is that we could be losing out on innovation by those small companies. NIH is setting things up by playing with the big kids and giving the cold shoulder to people with the 'harebrained' schemes."

And criticisms that the government is moving too slowly persist. "Those of us with AIDS are impatient," says Michael Callen of the People with AIDS Coalition. "We don't have the time to wait for the research systems already in place to move at the glacial pace for which bureaucracies are famous. The U.S. government's track record in terms of the treatments for AIDS is nothing short of scandalous."

Rochelle Diamond of NOGLSTP sees it all as a race against time. "My fear," she says, "is that if the AIDS numbers grow even more dramatically than they already have, and it spreads through the heterosexual population and there is still no cure, I'd expect you'd see more civilian concerns and demands for quarantine. At that point AIDS would no longer be so much a scientific issue as an ideological one."

Brick is sympathetic to all. "Everyone is beating a unique pathway through the woods with this effort," he says. "Of course we're all going to fumble and trip. No one's ever done this before."

So the pressure will continue as scientists like Fauci direct the war at a pace they consider maximum. Finding the AIDS cure is an exciting but painful chase. Organizational innovations are being developed. Hundreds of scientists have thrown themselves into it. Others, although willing, regret having left projects they were hoping to build careers on. Many feel AIDS research will contribute little truly basic knowledge to other fields.

The sniping continues even as scientists from academia, industry, and government display extraordinary teamwork at the expense of ego. At the same time, drug companies race to be first with the best treatment. There is tremendous potential for profit in successful products. Behind the chaos is an underlying order, which is to say a path toward a single overall goal.

Meanwhile, the public and the AIDS community have put science under an uncomfortable spotlight. The Whitehead Institute's David Baltimore, cochairman of the Institute of Medicine's AIDS panel, provided the trite but true bottom line to the situation last August. "The biomedical community," he said, "will be judged in the future by how we respond." □

The Business Response

Hundreds of concerns involved in development of vaccines, drugs, and diagnostic tests despite scientific, medical, and business uncertainties

Marc S. Reisch, C&EN New York

AIDS, like most human tragedies, has drawn the typical human response: a rallying around of those in a position to help. In the case of AIDS, this response has seen the buildup of a massive and what is becoming a reasonably well-coordinated cooperative effort to combat and control the disease. Business has been involved almost from the start.

In fact, AIDS is becoming a business opportunity for a significant number of venture capitalists and the small biotechnology firms they invest in, as well as for a host of pharmaceutical and large diversified companies. And drawing on either government funds or private capital, these businesses are working to develop the vaccines, drugs, and medical technology to handle those afflicted.

There is clearly great economic potential in AIDS. But that potential is very difficult to assess at this time for the longer term. This is primarily because of great uncertainty over the number of new cases of AIDS that will develop in the coming years, especially on a worldwide basis.

Data on the numbers of people who have been afflicted to date in this country are apparently quite precise. According to the Centers for Disease Control, the number of cases of full-blown AIDS in the U.S. is almost 45,000, with the number of deaths approaching 26,000.

What these numbers will grow to within the next few years is far less certain. CDC predicts a cumulative total of between 201,000 and 311,000 AIDS cases in the U.S. by 1991. It sets the most likely number at 270,000.

However, the former chief of epidemiology for CDC, Alexander D. Langmuir, believes that the AIDS epidemic will peak next year. Langmuir, who also founded CDC's Epidemic Intelligence Service, believes that AIDS will not spread generally to the heterosexual population in this country.

On the other hand, Surgeon General C. Everett Koop says that between 1 million and 1.5 million people currently are infected with the virus in this country. But he admits that number is speculative. It could be 400,000 or 4 million. Those estimates are based on very shaky evidence.

In another example of uncertainty, New York City officials have put the number of city residents infected with the AIDS virus as high as 600,000. But New York state officials estimate that there are only 400,000 infected persons in the entire state.

Global AIDS estimates also cover a wide range. For example, the World Health Organization says that 5 million to 10 million people are infected worldwide. It estimates 500,000 to 3 million people will develop the disease in the next five years.

According to a just-published study by management consultants Frost & Sullivan, more than 600 different companies in the U.S. are actively involved in programs linked to AIDS therapy or diagnostics. It estimates that the combined AIDS-related R&D expenditures of these companies exceed $500 million annually.

Frost & Sullivan's study predicts that sales of AIDS diagnostic tests will increase from about $35 million in 1985 to $65 million in 1987 and $135 million by 1989. It suggests that an erosion in selling prices after 1989 as a result of competition will shrink the market to $105 million by 1991. AIDS therapy products probably will increase from virtually nothing in 1985 to $964 million in 1991, the study predicts. Should the AIDS epidemic continue to spread rapidly, the study forecasts that sales of an AIDS vac-

Burroughs Wellcome worker inspects capsules containing zidovudine

cine could exceed $1 billion annually.

Among the companies searching for an effective AIDS vaccine in this potentially enormous market, MicroGeneSys has received FDA approval for Phase 1 clinical trial for its version of an AIDS vaccine. According to MicroGeneSys president and chairman Frank Volvovitz, Phase 1 testing of the company's VaxSyn HIV-1 experimental vaccine began in September and is expected to last six months to a year. The National Institutes of Health, he says, continues to seek suitable volunteers to test the vaccine.

MicroGeneSys, he says, is owned by a small group of investors, though the company has no corporate partners to date. To finance its development of an AIDS vaccine as well as to finance other vaccine developments, Volvovitz says the company is considering an "arrangement" with a larger company, and would consider offering company stock to the public in the future, though the company has no immediate plans to do so.

A great deal, of course, would depend on MicroGeneSys' success in getting beyond clinical trials of its AIDS vaccine and receiving FDA approval. The attractiveness of the company as an investment would depend in large measure on not just approval, which is in no way guaranteed, but on public health officials' determination of population groups who would benefit from receiving the vaccine. That could cover, says Volvovitz, "a broad range of individuals from high-risk groups to the whole population. A lot depends on public health policy, which we are not a part of."

Burroughs Wellcome, the company that developed and received approval for zidovudine (AZT), the first drug which has been shown to prolong the lives of some AIDS patients, does not break out its R&D costs for the drug. However, a spokesman for the company says that the firm did spend $80 million in raw material purchases and capital improvements in gearing up for manufacture. The cost of the drug to patients is between $7000 and $10,000 a year.

Zidovudine was first drug shown to prolong the lives of some AIDS patients

Burroughs Wellcome also markets other drugs to treat AIDS opportunistic infections. These include, says a company spokeswoman, Zovirax, a treatment for herpes, and Daroprim, a treatment for toxoplasmosis. She says that the company is also working with α-interferon for possible application to AIDS patients.

A Hoffmann-La Roche spokeswoman would say only that the company spends $2 million daily worldwide on the research and development of new drugs, with an unspecified amount in the AIDS area. However, the company is investigating a compound called dideoxycytidine (DDC) as a potential AIDS treatment now in Phase 1 testing. Hoffmann-La Roche also is developing interleukin-2, a human protein for use in combination with other AIDS drugs, in partnership with Immunex. It is also testing its brand of α-interferon to treat Kaposi's sarcoma.

Imreg, a small New Orleans-based concern, has developed Imreg-1, a biologic developed from the white blood cells of healthy individuals. According to Arthur Gottlieb, chief executive officer of Imreg and also chairman of microbiology and immunology at Tulane University's medical school, Imreg-1 helps weakened T-helper cells function more normally. Now in Phase 3 testing in 150 patients, Imreg-1 has so far shown that it supports the immune system and has helped some patients gain weight.

Gottlieb says that Imreg has not financed its advancements with federal money of any sort. It has, he says, raised $15 million over the past six years, primarily from the sale of stock. He estimates that development costs for Imreg-1 to this point are $8 million, far lower than development costs associated with most new drugs, mostly because Imreg-1 is a biologic.

Among companies marketing diagnostic tests for AIDS, Du Pont estimates the U.S. market at $150 million annually. Only six months ago, says the Du Pont spokesman, people thought this market was only $40 million and set the world market at $150 million. This change is due largely to a sharp increase in the estimate of the number of medical institutions, federal agencies, state agencies, and other groups that eventually will start AIDS testing programs. Tests that Du Pont distributes include a DNA probe kit produced by Molecular Biosystems and a Western blot test from American Bionetics. Du Pont is developing its own second-generation recombinant protein tests.

Sue Brown, a marketing manager for Organon Teknika, a U.S. unit of the Dutch company Akzo, says the size of the market for diagnostics could easily be $150 million annually. Brown also says that the dollar

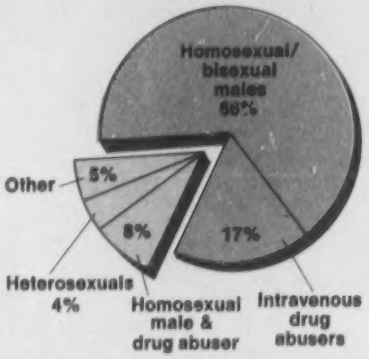
CDC constantly updates AIDS statistics

The Centers for Disease Control publishes weekly data on AIDS that offer fine detail of the distribution of the disease in this country. The bottom line, however, is the increasing numbers of new cases. These have grown from less than 300 in 1981 to more than 14,000 in 1986 and more than 8000 in the first half of this year.

Two thirds of the cases are homosexual males. One sixth are intravenous (IV) drug users, and another 8% are both homosexual males and IV drug abusers. Women make up 7% of all cases and 1% are children. What CDC describes as "heterosexual cases" make up 4% of the total to date. This category includes persons, both male and female, who have had heterosexual contact with a person with AIDS (or at high risk for AIDS) and persons born in countries in which heterosexual transmission is believed to play a major role. Almost one half, 49%, of females with AIDS are themselves IV drug users.

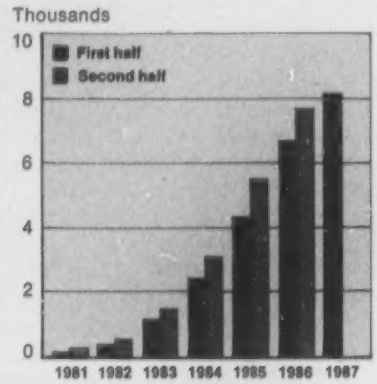
Only 5% of cases in the white population are drug abusers. In both the black and Hispanic populations, the figure is 35%. This approaches the male homosexual category of 40% for black, 49% for Hispanics.

Most are homosexual males, intravenous drug abusers



Total = 44,129 adult cases

Six-month figures show new cases of AIDS still growing



Source: Centers for Disease Control

figures are in constant flux as new tests and new clients enter the market. The company's own Bio-Enza-Bead HIV ELISA test can cost anywhere between $1.50 and $4.00 per sample tested not including labor, she says. Its main market is the 20 million units of blood annually collected in the U.S.

Organon Teknika recently signed a contract with Epitope, a Beaverton, Ore., biotechnology company, to distribute Epitope's Western blot HIV test kit. Epitope estimates that the international market for such an AIDS test is $20 million annually. Epitope has not yet received FDA approval for sale of its kit. It values its contract with Organon Teknika at $3 million per year.

According to the American Association of Blood Banks, all units of blood annually collected by blood banks are tested for AIDS antibodies. The screening of units for AIDS virus as well as recently added testing for hepatitis virus has added $1.00 or so to the unit cost of red blood cells, says an association spokeswoman. Units cost between $30 and $100, depending on the part of the country where they are sold.

Although a number of small companies continue to be involved in developing products for the AIDS market, many larger companies have worked out financial arrangements with much smaller concerns to get a start in the AIDS product markets. Those companies include Du Pont (with Centocor, Cistron, Molecular Biosystems, and others), Baxter-Travenol (with Cambridge Medical Tech, Ribi Immunochem, Biogen, and others), Hoffmann-La Roche (with Genentech, Immunex, and Centocor), and American Cyanamid (with Cytogen, Hybritech, Celltech, and others).

Eastman Kodak, for instance, has developed a distribution business in AIDS-related diagnostics and distributes an ELISA test developed by Cellular Products and Cetus. In addition, it plans to offer a gene amplication reference service using Cellular Products technology beginning in 1988, according to John G. Knowles, Eastman Kodak product manager of biological diagnostics.

The trend of smaller companies linking forces with larger companies with deep pockets is likely to continue. Because of the recent decline in the stock market, it has become less likely that small, financially shaky biotechnology companies will be able to raise the large amounts of money they need in the hope of developing products for an uncertain AIDS market. "Those people who are willing to risk the market will put their money into safer stocks," says David Webber, a biotechnology industry analyst with Jeffrey Casdin & Co. "It's a dark period now for biotechnology stocks. Collaborations with large concerns will keep some of them afloat," he says.

Certain product markets have grown as unintended beneficiaries of the AIDS scare. Hospital support staff, emergency medical workers, police, and dental hygienists have started to wear latex rubber gloves for protection from the AIDS virus. Industry sources say that manufacturers expect demand to double for latex gloves within the next three to four years.

Condom sales also have benefited from the AIDS scare. Most of the 12% growth in condom sales between July 1986 and July 1987 can be attributed to the Surgeon General's recommendation that condoms be used to reduce the risk of AIDS transmission, says a spokesman for Carter-Wallace, manufacturer of Trojan condoms. Partly as a result of the scare, too, condoms are now vended by supermarkets and convenience store outlets, helping increase unit sales to 365 million at a value of $200 million annually. □